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=> que L1

L2 QUE L1

=> d l1
L1 HAS NO ANSWERS
L1 STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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=> s l1
SAMPLE SEARCH INITIATED 11:37:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        0 TO ITERATE

100.0% PROCESSED        0 ITERATIONS                                 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
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L3            0 SEA SSS SAM L1

=> s l1s l1 full
COMBINATION OF STRUCTURE AND TEXT TERMS NOT VALID
The query entered contains both search terms created by
structure-building or screen commands and text search terms.  L#s
created via the STRUCTURE or SCREEN commands must be searched in the
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=> s l1 full
FULL SEARCH INITIATED 11:38:01 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -       34 TO ITERATE

100.0% PROCESSED       34 ITERATIONS                                10 ANSWERS
SEARCH TIME: 00.00.01

L4           10 SEA SSS FUL L1

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=> s l4
L5          13 L4

=> d cbib abs hitstr 1-13

L5   ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2008 ACS on STN
2006:1099787   Document No. 145:432242  Treatment of connective tissue diseases
     of the skin with β2-adrenoceptor agonists.  Weidner, Morten Sloth
     (Astion Development A/S, Den.).  PCT Int. Appl. WO 2006108424 A2 20061019,
     52pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,
     BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES,
     FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
     KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ,
     NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
     SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA; RW: AT,
     BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE,
     IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.  (English).
     CODEN: PIXXD2.  APPLICATION: WO 2006-DK50013 20060412.  PRIORITY: DK
     2005-529 20050413.
AB   The present invention provides effective and safe medicaments for the
     treatment of connective tissue diseases of the skin, particularly with
     respect to the treatment of cutaneous forms of Lupus Erythematosus.  The
     medicaments comprise as the therapeutically active ingredient a beta2
     adrenoceptor agonist.  The invention furthermore relates to dermatol.
     compns. without skin sensitization properties and which contain
     enantiomerically pure or enriched R-enantiomers of a beta2 adrenoceptor
     agonist.
IT   194785-31-4, KUR-1246
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (treatment of connective tissue diseases of skin with
        β2-adrenoceptor agonists)
RN   194785-31-4  CAPLUS
CN   Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-
     [4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-,
     sulfate (2:1) (salt) (9CI)  (CA INDEX NAME)

     CM   1

     CRN  194785-19-8
     CMF  C24 H32 N2 O5

Absolute stereochemistry.  Rotation (-).
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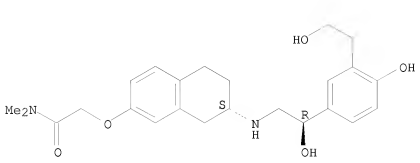


CM 2

CRN 7664-93-9
CMF H2 O4 S

L5 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
2006:331833 Document No. 145:241615 Effects of KUR-1246, a selective uterine relaxant, on transplacental passage and transmigration to milk. Furihata, Yoshio; Kobayashi, Mamoru; Kojima, Masami; Kobayashi, Kaoru; Kawarabayashi, Tatsuhiko; Yamamoto, Toshinori (Department of Clinical Pharmacy, School of Pharmaceutical Sciences, Showa University, Tokyo, Japan). Journal of Obstetrics and Gynaecology Research, 32(1), 4-9 (English) 2006. CODEN: JOGRFD. ISSN: 1341-8076. Publisher: Blackwell Publishing Asia Pty Ltd..

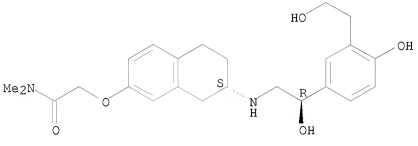
AB Aim: To evaluate the safety of KUR-1246 as a tocolytic agent, we determined the effects of its constant infusion on efficacy, transplacental passage, and transmigration to milk in pregnant or puerperal animals and compared them to the effects of ritodrine hydrochloride. Methods: A balloon method was used to evaluate the inhibitory effects of KUR-1246 constant infusion on spontaneous uterine motility in pregnant rats. We also measured transplacental passage and transmigration to milk of KUR-1246 in pregnant and/or puerperal animals. KUR-1246 and ritodrine hydrochloride concns. were quantified using a liquid chromatog.-tandem mass spectrometry method. Results: Constant infusion of KUR-1246 and ritodrine hydrochloride clearly inhibited spontaneous uterine motility in vivo. The ED50 value for KUR-1246 was 1.1 mg/kg/min, a potency which was approx. 40-fold greater than that of ritodrine hydrochloride. Transplacental passage (proportions of fetal plasma/maternal plasma) of KUR-1246 in pregnant rats and/or guinea pigs were approx. one-half to one-third of that of ritodrine hydrochloride. Transmigration of KUR-1246 to milk in puerperal rats disappeared by 48 h after injection. Conclusions: KUR-1246 is a promising drug for the treatment of preterm labor in obstetric practice because it is as efficacious as currently used agents yet less likely to produce direct effects on the fetus.

IT 194785-31-4, KUR1246
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(infusion of β2-adrenergic receptor agonist KUR-1246 inhibited spontaneous uterine motility in pregnant rat, guinea pig without adverse cardiovascular event like hypotension and tachycardia, show efficacy of tocolytic agent KUR1246)
RN 194785-31-4 CAPLUS
CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 194785-19-8
CMF C24 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 7664-93-9
CMF H2 O4 S

L5 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
2006:151612 Document No. 144:205706 Cardiovascular effects of KUR-1246, a new tetrahydronaphthalen derivative β2-adrenoceptor agonist and a selective uterine relaxant. Furihata, Yoshio; Motokawa, Yoshiyuki; Murata, Satoshi; Kiguchi, Sumiyoshi; Kobayashi, Mamoru; Murakami, Makoto; Kojima, Masami; Yamamoto, Toshinori (Department of Clinical Pharmacy, School of Pharmaceutical Sciences, Showa University, Tokyo, Japan). Arzneimittel Forschung, 56(1), 18-24 (English) 2006. CODEN: ARZNAD. ISSN: 0004-4172. Publisher: Editio Cantor Verlag.
AB The aim of this study was to assess the cardiovascular effects of KUR-1246

(CAS 194785-31-4, (-)-bis(2-{[(2S)-2-(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl}amino)-1,2,3,4-tetrahydronaphthalen-7-yl]oxy-N,N-dimethylacetamide monosulfate), a new β2-adrenoceptor agonist tocolytic agent. In conscious dogs, the i.v. administration of KUR-1246 at 0.1 and 1 μg/kg had no effects on blood pressure, heart rate or femoral artery blood flow. KUR-1246 at 10 and 100 μg/kg significantly decreased blood pressure and increased heart rate. In the electrocardiograms, KUR-1246 did not affect QT intervals or QTc. In addition, the cardiac effects of KUR-1246 were evaluated in in vitro electrophysiol. studies. KUR-1246 at 10 μmol/L did not affect action potential parameters (the maximal upstroke velocity, resting membrane potential, action potential amplitude and action potential durations) in isolated papillary muscles of guinea pigs or in the human ether-a-go-go related gene (HERG) tail current recorded from stably transfected human embryonic kidney (HEK) 293 cells. On the basis of these results, the effects of KUR-1246 in conscious dogs on the cardiovascular system appear to be limited to changes in blood pressure and heart rate. Therefore, KUR-1246 is unlikely to provoke ventricular arrhythmias by delaying the ventricular repolarization.

IT 194785-31-4, KUR-1246
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cardiovascular toxicity of tocolytic tetrahydronaphthalen derivative KUR-1246)

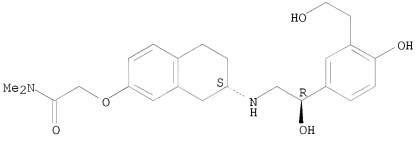
RN 194785-31-4 CAPLUS

CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 194785-19-8
CMF C24 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 7664-93-9
CMF H2 O4 S

L5 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN

2005:111451 Document No. 142:348973 Effects of long term administration of KUR-1246, a selective β2-adrenoceptor agonist, on pregnant sheep and their fetuses. Murata, Satoshi; Matsuda, Tadashi; Kiguchi, Sumiyoshi; Kobayashi, Mamoru; Cho, Kazutoshi; Okuyama, Kazuhiko (Pharmacology Research, R+D, Kissei Pharmaceutical Co., Ltd., Japan). BJOG, 112(1), 69-74 (English) 2005. CODEN: BIOGFQ. ISSN: 1470-0328. Publisher: Blackwell Publishing Ltd..

AB Objective: To evaluate the safety of KUR-1246 as a tocolytic agent, we examined the effects of its long term infusion on respiratory and cardiovascular systems and general metabolism in pregnant sheep and their fetuses. Design: Animal experiment with chronically instrumented ewes and their fetuses. Setting: Center for animal expts., Hokkaido University School of Medicine, Japan. Sample: Eight Suffolk ewes at 117 to 120 days of gestation. Methods: At 120-124 days of gestation, ewes (n = 4) were infused i.v. for 24 h with KUR-1246 at 0.03 μg/kg/min, a dose that completely inhibits oxytocin-induced uterine contractions in pregnant sheep. The controls received saline instead (n = 4). Statistical comparisons were carried out by repeated-measures ANOVA followed by Dunnett's test. Main outcome measures Maternal and fetal values of heart rate, blood pressure, plasma electrolytes, glucose, insulin and non-esterified fatty acid levels, and blood gases and lactate level. Results: The maternal plasma levels of KUR-1246 increased and reached a plateau at 15 h or later from the start of the infusion, whereas the fetal levels of it were below the lower limit of quantification (0.1 ng/mL) throughout the experiment Significant differences over time between the ewes that had received with KUR-1246 and the controls were found for the following parameters: maternal heart rate, blood lactate, plasma glucose, and plasma insulin levels, and fetal plasma glucose and plasma insulin levels ($P < 0.05$). In the KUR-1246 treated ewes, significant changes from the pre-infusion value were detected in maternal blood lactate and fetal plasma glucose levels within 6 h from the start of the infusion ($P < 0.05$). No significant differences were observed in other parameters in either ewes or fetuses. Conclusion: The physiol. changes induced by a 24-h infusion of KUR-1246 were transient and considered to be within the compensatory capacity in both pregnant ewes and their fetuses, suggesting that KUR-1246 is a potentially safe tocolytic agent for use by long term infusion.

IT 194785-31-4, KUR-1246
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long term infusion of KUR-1246 raised plasma level, blood lactate in pregnant ewes, fetal plasma glucose but no effect on heart rate, blood pressure, gases, plasma electrolyte suggest it is safe tocolytic agent for use by long term infusion)

RN 194785-31-4 CAPLUS

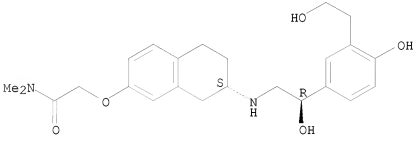
CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-,

sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 194785-19-8
CMF C24 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 7664-93-9
CMF H2 O4 S

L5 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
2004:633517 Document No. 141:134133 Preventive or remedy for intrauterine late embryonic development or pregnancy toxemia. Kobayashi, Mamoru; Murata, Satoru; Tsukahara, Yoshimi (Kissei Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 2004064825 A1 20040805, 15 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2004-JP355 20040119. PRIORITY: JP 2003-12947 20030122.

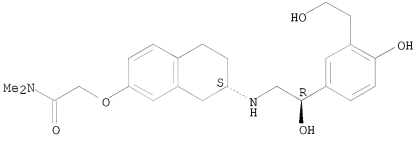
AB A preventive or a remedy for intrauterine late embryonic development or pregnancy toxemia contains, as the active ingredient, 2-[[(2S)-2-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-1,2,3,4-tetrahydronaphthalene-7-yl]oxy]-N,N-dimethylacetamide or a pharmacol. acceptable salt (sulfate, etc.) thereof which has a remarkable improving effect on embryonic body loss and congestive necrosis in distal portion in the extremities and a remarkable improving effect on an increase in

maternal urinary protein level or plasma neutral fat level with lessened fear for the loads on the mother body such as pulsation. Examples of the administration form thereof include tablets, capsules, injections and so on. Examples of diseases to be treated thereby include intrauterine late embryonic development caused by malnutrition and hyperlipemia accompanying pregnancy toxemia.

IT 194785-19-8 194785-31-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preventive or remedy for intrauterine late embryonic development or pregnancy toxemia)

RN 194785-19-8 CAPLUS
CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

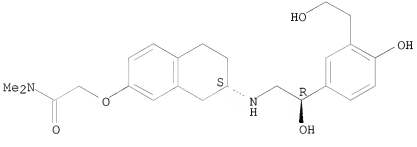


RN 194785-31-4 CAPLUS
CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 194785-19-8
CMF C24 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 7664-93-9
CMF H2 O4 S

Dates good below this line

2003:355016 Document No. 139:323296 Asymmetric borane reduction of prochiral ketone using chiral bis(α,α-diphenyl-2-pyrrolidinemethanol) carbonate. Yanagi, Takashi; Kikuchi, Ken; Takeuchi, Hideki; Ishikawa, Takehiro; Nishimura, Toshihiro; Kubota, Minoru; Yamamoto, Iwao (Central Research Laboratories, Kissei Pharmaceutical Co., Ltd., Nagano, 399-8304, Japan). Chemical & Pharmaceutical Bulletin, 51(2), 221-223 (English) 2003. CODEN: CPBTAL. ISSN: 0009-2363. OTHER SOURCES: CASREACT 139:323296. Publisher: Pharmaceutical Society of Japan.

AB Chiral bis(α,α-diphenyl-2-pyrrolidinemethanol) carbonate is a useful asym. auxiliary for the asym. borane reduction of prochiral ketones. Chiral bis(α,α-diphenyl-2-pyrrolidinemethanol) carbonate is recoverable from the reaction and directly reusable for the reaction. The intermediate of KUR-1246, which is being developed as a new uterine relaxant, was synthesized using the methodol. The reduction of 5-(bromoacetyl)-2-(phenylmethoxy)benzeneacetic acid Me ester using (R)-α,α-diphenyl-2-pyrrolidinemethanol carbonate (2:1) and borane-dimethyl sulfide gave (-)-5-[(1R)-2-bromo-1-hydroxyethyl]-2-(phenylmethoxy)benzeneethanol stereoselectively in 91% yield and in 99% enantiomeric excess.

IT 194785-31-4DP, KUR-1246, intermediates
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. borane reduction of prochiral ketone using chiral bis(α,α-diphenyl-2-pyrrolidinemethanol) carbonate)

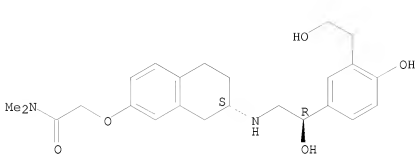
RN 194785-31-4 CAPLUS

CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 194785-19-8
CMF C24 H32 N2 O5

Absolute stereochemistry. Rotation (-).

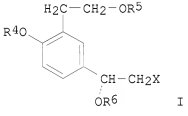


CM 2

CRN 7664-93-9
CMF H2 O4 S

L5 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
2002:792262 Document No. 137:294773 Preparation of optically active protected hydroxyphenylethyl halides and [(hydroxyphenylethylamino)naphthalenyloxy]acetamide as β2-adrenaline receptor stimulants. Yanagi, Takashi; Kikuchi, Takeshi; Takeuchi, Hideki; Ishikawa, Takehiro; Nishimura, Toshihiro (Kissei Pharmaceutical Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 2002302464 A 20021018, 12 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 2001-104314 20010403.

GI



AB 2-[(2S)-2-[[(2R)-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]-2-hydroxyethyl]amino]-1,2,3,4-tetrahydronaphthalen-7-yloxy]-N,N-dimethylacetamide (I) or its pharmaceutically acceptable salts are prepared by reaction of halohydrines II (R4-R6 = OH-protecting group; X = halo) with 2-[(2S)-2-amino-1,2,3,4-tetrahydronaphthalen-7-yloxy]-N,N-

dimethylacetamide (III), deprotection, and optionally reaction to prepare its salts. I is useful for treatment of threatened abortion, premature delivery, and urolithiasis and bronchodilators. (1R)-1-[4-benzyloxy-3-(2-tert-butyldimethylsilyloxyethyl)phenyl]-2-bromo-1-tert-butyldimethylsilyloxyethane (58.2 g) was reacted with 30.2 g III hydrochloride in the presence of K2CO3 in DMA at 120° for 6 h to give 68.6 g 2-[(2S)-2-[[(2R)-2-[4-benzyloxy-3-(2-tert-butyldimethylsilyloxyethyl)phenyl]-2-tert-butyldimethylsilyloxyethyl]amino]-1,2,3,4-tetrahydronaphthalen-7-yloxy]-N,N-dimethylacetamide, which was deprotected and treated with HCl to give I hemisulfate.

IT 194785-31-4P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of optically active protected hydroxyphenylethyl halides and [(hydroxyphenylethylamino)naphthalenyloxy]acetamide as β2-adrenaline receptor stimulants)

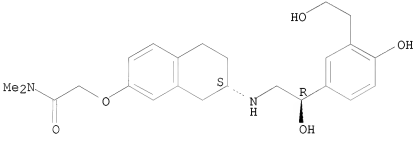
RN 194785-31-4 CAPLUS

CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 194785-19-8
CMF C24 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 7664-93-9
CMF H2 O4 S

L5 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
2002:666359 Document No. 138:297564 KUR-1246, a novel β2-adrenoceptor agonist, as a tocolytic agent. Kiguchi, Sumiyoshi; Matsuda, Tadashi; Cho, Kazutoshi; Okuyama, Kazuhiko; Akahane, Masuo; Fujimoto, Seiichiro (Pharmacology Research Laboratory, Research and Development, Kissei Pharmaceutical Co. Ltd., Matsumoto City, Japan). Obstetrics & Gynecology (New York, NY, United States), 100(3), 487-494 (English) 2002. CODEN: OBGNAS. ISSN: 0029-7844. Publisher: Elsevier Science Inc..

AB The objective of this study was to examine the effects of KUR-1246 on oxytocin-induced uterine contractions, the cardiovascular system, and general metabolism of pregnant sheep and their fetuses. At 123-125 days' gestation, ewes (n = 8) were infused with oxytocin (1.0 mU/kg/min) to induce uterine contractions. One hour later, KUR-1246 was infused for 3 consecutive hours beginning at a dose of 0.001 μg/kg/min for 30 min and increasing stepwise every 30 min to 0.3 μg/kg/min in the KUR-1246 group (n = 4). The control received saline instead (n = 4). Statistical comparisons of changes with time in the physiol. parameters between the two groups were carried out (anal. of variance). KUR-1246 suppressed oxytocin-induced uterine contractions more than 90% at doses over 0.03 μg/kg/min. Significant differences between the two groups were found at high doses over 0.03 μg/kg/min for the following parameters: maternal heart rate, diastolic blood pressure, mean blood pressure, base excess, blood K+, blood lactate, plasma glucose, plasma insulin, plasma non-esterified fatty acid levels, and fetal plasma glucose and plasma insulin levels. KUR-1246 significantly inhibited oxytocin-induced uterine contractions at doses over 0.03 μg/kg/min and showed reduced cardiovascular and metabolic side effects compared with ritodrine hydrochloride studied earlier in pregnant sheep.

IT 194785-31-4, KUR-1246
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(KUR-1246, a novel β2-adrenoceptor agonist, as a tocolytic agent)

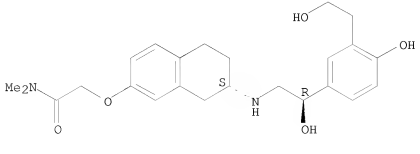
RN 194785-31-4 CAPLUS

CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 194785-19-8
CMF C24 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 7664-93-9
CMF H2 O4 S

L5 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
2002:463990 Document No. 138:49818 Diversity of inhibitory responses to β2-stimulants shown by term-pregnant human myometria in vitro is partly due to differences in receptor density. Sakakibara, Tomoko; Inoue, Yoshibito; Uzue, Satoshi; Tsukamoto, Takuji; Kobayashi, Mamoru; Kojima, Masami; Akabane, Masuo; Kitamura, Kenji; Kawarbayashi, Tatsuhiko (Department of Obstetrics and Gynecology, School of Medicine, Fukuoka University, Fukuoka, Japan). American Journal of Obstetrics and Gynecology, 186(5), 997-1004 (English) 2002. CODEN: AJOGAH. ISSN: 0002-9378. Publisher: Mosby, Inc..

AB Objective: The aims of this study were (1) to evaluate the usefulness of the new β2-adrenergic stimulant KUR-1246 as a tocolytic agent and (2) to clarify the mechanisms that underlie the diverse inhibitory effects of β2-stimulants that are seen in human myometria in vitro. Study design: The displacement of tritiated ([3H])(-)CGP 12177 (0.4 nmol/L) by KUR-1246 and other β2-stimulants was examined with human β1- and β2-receptors present on membrane fractions. The inhibitory effects of these β2-stimulants on the term-pregnant human myometrium were compared with the use of isometric tension recording and microelectrode methods. Finally, the relationship between [3H]dihydroaloprenolol binding and the magnitude of the tocolytic effect of isoproterenol was examined Results: KUR-1246 was approx. 80 times and 7 times more selective for β2-receptors than isoproterenol and ritodrine, resp. The inhibitory effect of KUR-1246 was as strong as the inhibitory effect of the conventional β2-adrenergic stimulants. A wide range of inhibitory effects was observed, even when high concns. of isoproterenol or KUR-1246 were applied. There was a correlation between the degree to which isoproterenol suppressed contractions and the number of [3H]dihydroaloprenolol binding sites on the membrane in each muscle strip. Conclusion: KUR-1246 should be a very useful β2-adrenergic stimulant for use as a tocolytic agent because of its high selectivity for the β2-receptor and its potent inhibitory effect. The diversity of the inhibitory effects that are induced by β2-stimulants is at least partly due to differences in β2-receptor d. among term-pregnant human myometria.

IT 194785-31-4, KUR-1246
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diversity of inhibitory responses to β2-stimulants in term-pregnant human myometria)

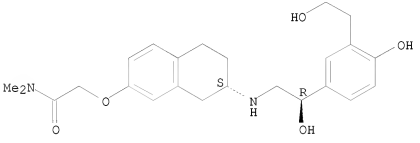
RN 194785-31-4 CAPLUS

CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 194785-19-8
CMF C24 H32 N2 O5

Absolute stereochemistry. Rotation (-).



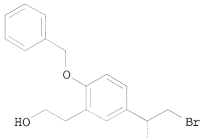
CM 2

CRN 7664-93-9
CMF H2 O4 S

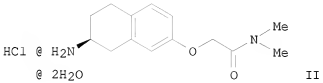
L5 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
2001:584506 Document No. 135:344264 The practical synthesis of a uterine relaxant, bis(2-{[(2S)-2-({(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)-phenyl]ethyl}amino)-1,2,3,4-tetrahydronaphthalen-7-yl]oxy}-N,N-dimethylacetamide) sulfate (KUR-1246). Yanagi, Takashi; Kikuchi, Ken; Takeuchi, Hideki; Ishikawa, Takehiro; Nishimura, Toshihiro; Yamamoto, Iwao (Central Research Laboratories, Kissei Pharmaceutical Co., Ltd., Nagano, 399-8304, Japan). Chemical & Pharmaceutical Bulletin, 49(8), 1018-1023 (English) 2001. CODEN: CPBTAL. ISSN: 0009-2363. OTHER SOURCES: CASREACT 135:344264. Publisher: Pharmaceutical Society of Japan.
GI

Print selected from Online session

Used reference



I



II

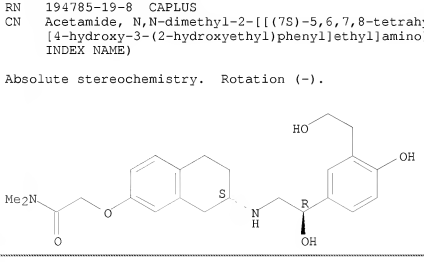
AB The synthetic route for a uterine relaxant, bis(2-{[(2S)-2-({(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl}amino)-1,2,3,4-tetrahydronaphthalen-7-yl]oxy}-N,N-dimethylacetamide) sulfate (KUR-1246), was established by the coupling of optically active components, bromohydrin I and amine II. The authors describe the practical synthesis of these two optically active components. I was obtained by the asym. borane reduction of the prochiral phenacyl bromide using a catalyst prepared from Al(OEt)3 and a chiral amino alc. Structural data of I were determined [monoclinic, P2, a 4.985, b 11.139, c 14.445Å, α 90.000, β 94.586, γ 90.000°, V 799.55 Å3, Z 2]. The other optically active component II was prepared from (S)-2-amino-7-methoxytetraline.

IT 194785-19-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation of uterine relaxant KUR-1246)

RN 194785-19-8 CAPLUS

CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

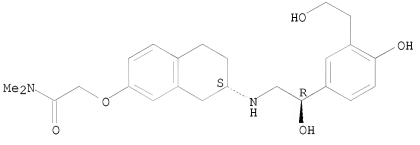


IT 194785-31-4P, KUR 1246
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of uterine relaxant KUR-1246)
RN 194785-31-4 CAPLUS
CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 194785-19-8
CMF C24 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 7664-93-9
CMF H2 O4 S

L5 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
2001:321635 Document No. 135:132305 Pharmacological characterization of KUR-1246, a selective uterine relaxant. Kobayashi, Mamoru; Takeda, Keiko; Murata, Satoshi; Kojima, Masami; Akahane, Masuo; Inoue, Yoshihito; Kitamura, Kenji; Kawarabayashi, Tatsuhiko (Pharmacology Research, R&D, Kissei Pharmaceutical Co., Ltd., Nagano, Japan). Journal of Pharmacology and Experimental Therapeutics, 297(2), 666-671 (English) 2001. CODEN: JPETAB. ISSN: 0022-3565. Publisher: American Society for Pharmacology and Experimental Therapeutics.

Used reference

AB The aim of the present study was to evaluate the efficacy and β2-adrenoceptor (AR) selectivity of KUR-1246, a new uterine relaxant. Inhibition of spontaneous or drug-induced uterine contractions by KUR-1246 was evaluated in pregnant rats and rabbits by an organ bath method or by a balloon method. The selectivity of KUR-1246 was assessed simultaneously

in organs isolated from late-pregnant rats. The affinity of KUR-1246 for human β1-, β2-, and β3-ARs was determined using two radioligands. KUR-1246 suppressed both spontaneous and drug-induced contractions in isolated uteri, the rank order of potency being isoproterenol > KUR-1246 > terbutaline > ritodrine. ICI-118551 (selective β2-AR antagonist) competitively antagonized the KUR-1246-induced inhibition of spontaneous uterine contractions, but CGP-20712A (selective β1-AR antagonist) and SR-58894A (selective β3-AR antagonist) did not. All β-AR agonists tested produced significant inhibition of spontaneous uterine contractions in vivo: ED30 value for KUR-1246 was 0.13 μg/kg/min, a potency about 6 times and 400 times greater than that of terbutaline and ritodrine, resp. In contrast, the pos. chronotropic effect was minimal in KUR-1246-treated rats. KUR-1246 displaced radioligand binding to β1-, β2-, and β3-ARs, the pKi values being 5.75±0.03, 7.59±0.08, and 4.75±0.03 for β1-, β2-, and β3-ARs, resp. For the selectivity of KUR-1246 for human β2-AR, we obtained values of 39.2 ([IC50 for β1-AR]/[IC50 for β2-AR]) and 198.2 ([IC50 for β3-AR]/[IC50 for β2-AR]), indicating an apparently higher affinity for human β2-AR than for other β-AR subtypes. The present study clearly demonstrated that KUR-1246 is a more selective β2-AR agonist than the drugs presently used for relaxing uterine muscle.

IT 194785-31-4, KUR 1246
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(uterine relaxant action of KUR-1246 and selectivity for β2-adrenoceptor)

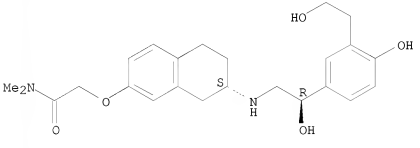
RN 194785-31-4 CAPLUS

CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 194785-19-8
CMF C24 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

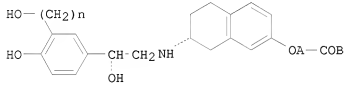
CRN 7664-93-9

Print selected from Online session

CMF H2 O4 S

L5 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
1999:136878 Document No. 130:196510 Preparation of phenylethanolaminotetralin derivatives as bronchodilators. Tamai, Tetsuro; Tanaka, Nobuyuki; Muranaka, Hideyuki; Kikuchi, Ken; Tsutsumi, Naoyuki; Akahane, Masuo (Kissei Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 9909001 A1 19990225, 31 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1998-JP3545 19980810. PRIORITY: JP 1997-259233 19970819.

GI



I

AB Phenylethanolaminotetralin derivs. represented by general formula (I) and pharmacol. acceptable salts thereof [wherein A represents lower alkylene; B represents amino, di(lower alkyl)amino or 3- to 7-membered alicyclic amino optionally containing oxygen; n is an integer of 1 or 2] are prepared They stimulate β2-adrenaline receptors with very weak β1-adrenaline receptor-stimulating activity (effect on heart), have potent and selective bronchodilating effects, and are highly useful as bronchodilators for the treatment and prevention of respiratory tract congestion and bronchostenosis (bronchiostenosis). Thus, (-)-(R)-2-(2,2-dimethylbenzo[1,2-d]-1,3-dioxan-6-yl)-2-hydroxyacetic acid (preparation given) was condensed with (R)-2-amino-7-hydroxytetralin hydrobromide using (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate and ET3N in DMF at room temperature for 14 h to give the hydroxyacetamide derivative followed by reduction with boron-dimethylsulfide complex to the ethanolamine derivative and N-alkylation with 2-bromo-N,N-dimethylacetamide to give the title compound I (A-COB = Ch2CONMe2, n = 1) (II). II in vitro showed EC50 (50% relaxant activity of

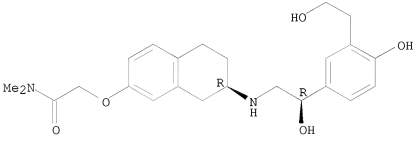
phosphocholine) of 2.5+10-10 M for relaxing the histamine-induced contraction of a strip-chain of rings prepared from Hartley guinea pig air way.

IT 220639-97-4P 220639-98-5P 220639-99-6P
220640-00-6P 220640-01-7P 220640-02-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylethanolaminotetralin derivs. as bronchodilators for treatment and prevention of respiratory tract congestion and bronchostenosis)

RN 220639-97-4 CAPLUS

CN Acetamide, N,N-dimethyl-2-[[(7R)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



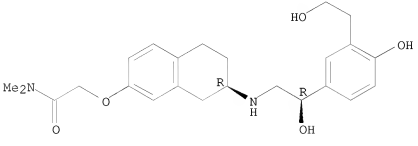
RN 220639-98-5 CAPLUS

CN Acetamide, N,N-dimethyl-2-[[(7R)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220639-97-4
CMF C24 H32 N2 O5

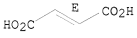
Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

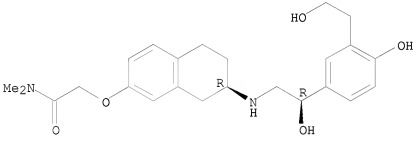


RN 220639-99-6 CAPLUS
CN Acetamide, N,N-dimethyl-2-[[(7R)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220639-97-4
CMF C24 H32 N2 O5

Absolute stereochemistry. Rotation (+).

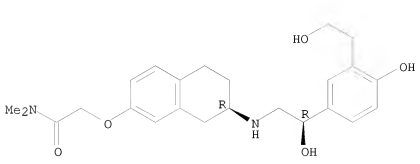


CM 2

CRN 7664-93-9
CMF H2 O4 S

RN 220640-00-6 CAPLUS
CN Acetamide, N,N-dimethyl-2-[[(7R)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, monohydrochloride (9CI) (CA INDEX NAME)

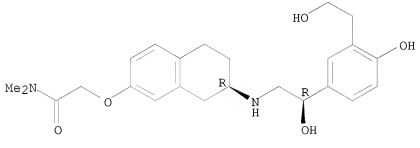
Absolute stereochemistry. Rotation (+).



● HCl

RN 220640-01-7 CAPLUS
CN Acetamide, N,N-dimethyl-2-[[(7R)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, monohydrobromide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



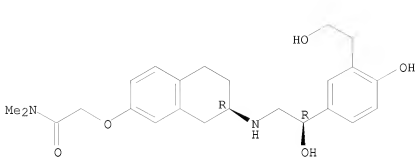
● HBr

RN 220640-02-8 CAPLUS
CN Acetamide, N,N-dimethyl-2-[[(7R)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220639-97-4
CMF C24 H32 N2 O5

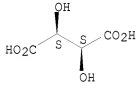
Absolute stereochemistry. Rotation (+).



CM 2

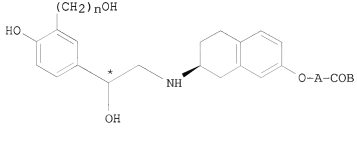
CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



L5 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
1997:563096 Document No. 127:205361 Preparation of 3,4-disubstituted phenylethanolaminotetralincarboxamide derivatives having a selective β2-adrenergic receptor stimulating effect. Kitazawa, Makio; Okazaki, Kosuke; Tamai, Tetsuro; Saito, Masaru; Tanaka, Nobuyuki; Kobayashi, Hiroaki; Kikuchi, Ken; Muranaka, Hideyuki (Kissei Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 9730023 A1 19970821, 69 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1997-JP424 19970218. PRIORITY: JP 1996-68885 19960219.

GI



I

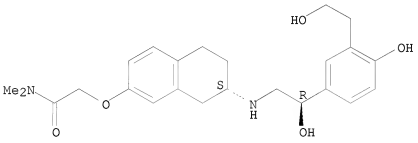
AB The title 2-(2-phenyl-2-hydroxyethylamino)tetralin-7-yloxyalkylcarboxamide derivs. represented by general formula (I; lower alkylene; B = amino, di(lower alkyl)amino or 3- to 7-membered alicyclic amino optionally containing oxygen in the ring; n = an integer of 1 or 2; the carbon atom marked with * means a carbon atom with the R or S configuration or a mixture thereof) and their pharmacol. acceptable salts having a selective β2-adrenergic receptor stimulating effect with a relieved burden on the heart such as frequent pulse (no data) are prepared These compds. are useful as preventives for threatened abortion/premature birth, bronchodilators and pain-relieving and urinary calculus (lithangiurea) agents in ureterolithiasis. Thus, 2.00 g Et tetralin-7-yloxyacetate derivative I (A = CH2, B = OEt, n = 1) and 17.9 g Me2NH were dissolved in a sealed tube and heated at 65° for 36 h to give I (A = CH2, B = NMe2, n = 1).

IT 194785-19-8P 194785-20-1P 194785-21-2P
194785-31-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylethanolaminotetralincarboxamide derivs. as selective β2-adrenergic receptor agonists)

RN 194785-19-8 CAPLUS

CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]- (CA INDEX NAME)

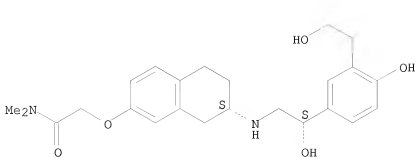
Absolute stereochemistry. Rotation (-).



RN 194785-20-1 CAPLUS

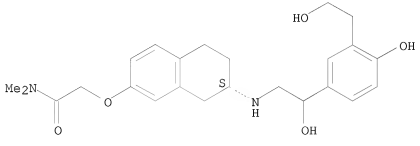
CN Acetamide, N,N-dimethyl-2-[[5,6,7,8-tetrahydro-7-[[2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, [S-(R*,R*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 194785-21-2 CAPLUS
CN Acetamide, N,N-dimethyl-2-[[5,6,7,8-tetrahydro-7-[[2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, (7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

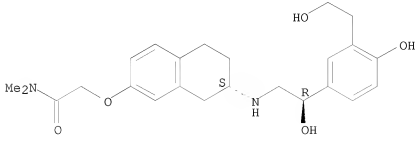


RN 194785-31-4 CAPLUS
CN Acetamide, N,N-dimethyl-2-[[(7S)-5,6,7,8-tetrahydro-7-[[(2R)-2-hydroxy-2-[4-hydroxy-3-(2-hydroxyethyl)phenyl]ethyl]amino]-2-naphthalenyl]oxy]-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 194785-19-8
CMF C24 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 7664-93-9
CMF H2 O4 S